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EXAMINER

MONDESI, ROBERT B

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1653

DATE MAILED: 05/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/735,418

Applicant(s)

REED ET AL.

Examiner

Robert B. Mondesi

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1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above claim(s) 1-17,20,22 and 34-37 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 23,27,29,32 and 33 is/are allowed.
- 6) ☒ Claim(s) 18,19,21,24-26,30,31 and 39 is/are rejected.
- 7) ☒ Claim(s) 28,38 and 40-45 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 June 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office action is in response to the amendment filed March 07, 2005. **Claims 38-45** are new. **Claims 1-45** are pending. **Claims 19, 21, 23-33, and 38-45** as drawn to elected Invention VI are presently under examination.

Withdrawal of Objections and Rejections

The rejection of **claims 21, 24-28, 30 and 33** under 35 U.S.C § 112, second paragraph is withdrawn.

The rejection of **claims 21, 24-30 and 32** under 35 U.S.C. 102(b) as being anticipated by Petros et al., 2000 is withdrawn.

Maintenance of rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 24-26 and 30 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was explained in the previous Office action.

Claims 19, 21 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection is maintained because presently portion of the claim reads “comprising screening compounds using BLANK for binding to ...”, the act of simply deleting NMR has not further explained “using” and in fact it has made the claim more ambiguous, since it is no longer understood what is being used to screen compounds with.

Claim Rejections - 35 USC § 102

Claims 18 and 31 remain rejected under 35 U.S.C. 102(b) as being anticipated by Li et al.

This rejection was explained in the previous Office action.

Response to applicant's arguments

In regards to the rejection of claims 24-26 and 30 as not complying with the written description requirement, the applicants assert that the claims have been amended to include functional language that require the polypeptide to possess a specific biological activity, i.e.; the ability to bind Bcl-2 and modulate its activity so as to induce apoptosis; therefore there is no substantial variability that falls within the species which fall within the scope of the claim. Furthermore, the structure of the fragment in claims 25 and 26 are disclosed in the specification for example at page X, and paragraph X!!!

Applicants assert further that there is extensive support in the specification as filed for functional derivatives and natural variants which are inductive of apoptosis, including: example 3 which provides methods of testing compounds for the function, Example 7 and other parts of the specification which provide mutants which remove all

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or part of the DNA-binding domain and fragments which include the DC1 region of TR3; Example 6, 7, 8 and 9 which provide methods for screening peptides; and structural-based drug design; all of which can be used to identify functional derivatives and natural variants.

Applicants' arguments have not been found persuasive because the applicants have not provided for an association of the structure of the fragment with function (biological activity). In another words the applicants have not described the structural characteristics of the mentioned species that contributes to the biological activity of the functional fragment of TR3, that in effect leads to Bcl-2 binding and hence is inductive of apoptosis. The mentioned examples 6-9 are methods that investigate further the mentioned biological activity that may be associated with a given fragment but neither describes which portion of the TR3 fragment is responsible for the biological activity. Furthermore the examiner does not understand what is meant by page X, paragraph X since the specification is not numbered using Roman numerals.

Applicants urge that claim 18 is drawn to: a method of identifying molecules that induce apoptosis by determining the ability of the molecules to bind to Bcl-2-family protein in the loop region and modulate the activity of said protein so as to be inductive of apoptosis and with respect to claim 18, Li et al. do not anticipate identifying a molecule which binds to the loop reign of Bcl-2 or family member, because the importance of the loop region was not recognized in the prior art. In regards to claim 31,

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the applicants urge that Li et al. do not provide any language to suggest that the two hybrid system included a Bcl-2 family domain protein.

Applicants arguments have not been found persuasive because the prior art does recognize the importance of the loop region of the Bcl-2 family, Petros et al., cited in the previous office action, teach that the structure of Bcl-xL (a Bcl-2 family protein) consists of eight alpha-helices connected by loops and the loops between helix 3 and 4, helix 4 and 5, and helix 5 and 6 consist of 14, 4 and 3 residues, respectively, and in each case, the loops allow nearly 180 degrees chain reversal. Petros et al. teach further that the binding site for the Bad peptide is a groove lined with hydrophobic side chains formed predominantly by helix 2, 3, 4 and 8, and the four-residue loop connecting helix 4 to helix 5 (page 2529, column 2, lines 1-5); and therefore clearly the prior art recognizes the importance of the loop region.

In response to applicants' assertions in regards to claim 31 the examiner would like to direct the applicants' attention to column 2, lines 1-4 of the third paragraph on page 47542, wherein Li et al. teach that in order to explore the apoptosis regulatory mechanism related to Bcl-2 family membrane proteins, a search was conducted for proteins that interacted with myeloid cell leukemia protein 1 (MCL1), a Bcl-2 homologue, using the yeast two hybrid system.

New rejection(s) and Objections

Claim Objections

Claim 28 objected to because of the following informalities: In **claim 28** the applicants have inadvertently deleted "wherein", an amendment to the claim reinserting wherein will over come the objection.. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 is an independent claim; therefore TCTP needs to be spelled out in the first instance of use.

Conclusion

Claims 18-19, 21, 24-26, 30-31 and 39 are rejected.

Claims 28 and 38 and 40-45 are objected. **Claim 38 and 40-45** are objected to for depending from a rejected base claim.

Claims 23, 27, 29, 32-33 are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Robert B. Mondesi
Patent Examiner
Group 1653

04-29-05


ROBERT A. WAX
PRIMARY EXAMINER

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